Table 2
Results for Pain, Stiffness and Function

Study	Trials N	Patients N	Effect Size	I^2
Pain				
All timepoints	5	712	-0.07 (-0.24, 0.10)	16%, low
4 weeks	3	547	0.01 (-0.15, 0.18)	0%, no
12 weeks	4	541	-0.05 (-0.28, 0.17)	30%, low
Stiffness	2	159	0.03 (-0.27, 0.34)	0%, no
Function	2	159	-0.08 (-0.39, 0.23)	0%, no

Note: CI = Confidence Interval; I^2 = Heterogeneity Score

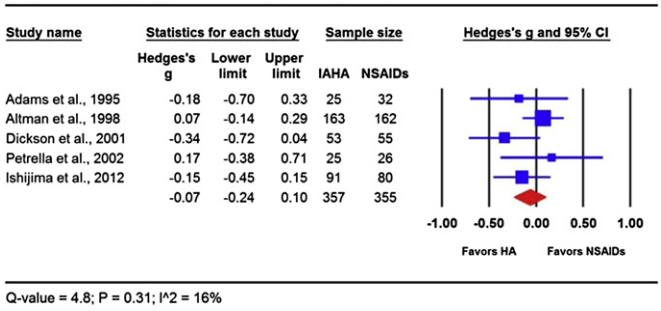

Figure 1. Forest plot for pain at the end of the trial.

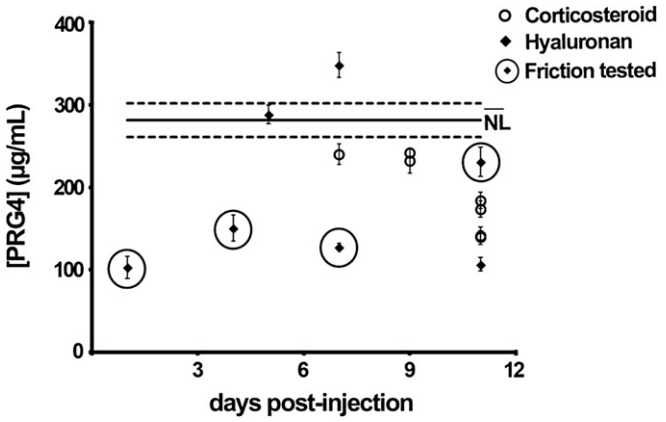

Figure 1. [PRG4] in flare-SF after IA HA or corticosteroid injection. [PRG4] ±SEM in normal (NL) SF (N=29) shown by black lines. Samples selected for friction testing (HA flare only) are circled.

584

EFFECT OF FLARE REACTION TO INTRA-ARTICULAR INJECTION ON CARTILAGE LUBRICATING ABILITY OF HUMAN SYNOVIAL FLUID

T.E. Ludwig, J.R. McAllister, V.M. Lun, J.P. Wiley, T.A. Schmidt. *Univ. of Calgary, Calgary, AB, Canada*

Purpose: In synovial fluid (SF), proteoglycan 4 (PRG4) and hyaluronan (HA) act synergistically to contribute to the boundary lubrication of articular cartilage in a dose-dependent manner. Alterations in PRG4 and HA levels in SF can lead to compromised boundary lubrication, which can be restored in vitro by lubricant supplementation. Intra-articular (IA) injections of HA and corticosteroid are common treatments for osteoarthritis (OA). In vitro studies have suggested that IA HA alone may be insufficient to provide chondroprotection, as evidenced by increased chondrocyte apoptosis during cartilage-on-cartilage friction testing relative to native SF. A recent review highlighted the small benefit of IA HA treatment and increased risk of flare reaction (defined as a hot, painful, swollen knee after injection). The effects of a reaction to IA treatment on SF lubricant content and lubricating ability are unknown. The objectives of this study were to 1) quantify PRG4 and HA content in OA SF after a flare reaction to IA treatment and 2) assess the cartilage boundary lubricating ability of flare-SF deficient in PRG4, with and without supplementation with PRG4±HA.
Methods: Knee SF was collected from OA patients' requiring aspiration after corticosteroid or HA injection (≤11 days after injection, N = 14.) PRG4 and HA concentrations in normal (NL, N = 29) and flare-SF were measured by sandwich enzyme linked immunosorbent assay. HA molecular weight (MW) distribution was determined by agarose gel electrophoresis. Lubricating ability of PRG4-deficient flare-SF, PRG4-deficient flare-SF supplemented with normal levels of PRG4±HA, and NL SF was tested in a normal human cartilage-on-cartilage friction test. Static, µstatic,Neq, and kinetic, <µkinetic,Neq>, friction coefficients were calculated.
Results: Flare-SF PRG4 and HA concentrations ranged from below normal to super-physiological. Four samples deficient in PRG4 ([PRG4], below the average NL concentration) were selected for friction testing; all 4 were reactions to IA HA (Fig. 1). HA concentration in the friction tested flare-SF did not differ from NL (p=0.5, not shown), while HA MW was shifted slightly towards the smaller size range (Fig. 2). <µkinetic,Neq> in PRG4-deficient flare-SF (Fig. 3) was not altered compared to NL, and no changes were observed with PRG4 or PRG4+HA supplementation (p=0.77-1.0).
Conclusions: These results demonstrate that some flare-SF exhibits altered lubricant composition after reaction to IA injection, as has been previously observed in ACL injury and chronic OA, but can still retain normal boundary lubricating ability. A dramatic shift towards lower HA MW in chronic OA SF deficient in PRG4 has previously been observed; an HA distribution closer to normal SF, as observed here, could contribute to the normal lubricating ability observed. Other characteristics of PRG4, including glycosylation and size distribution, remain to be evaluated and compared between healthy and diseased SF, and may have effects on SF lubricating ability. Evaluation of OA SF after IA injection over a longer time course, along with further analysis of PRG4 characteristics, will provide further insight into effects of inflammation on joint lubrication.

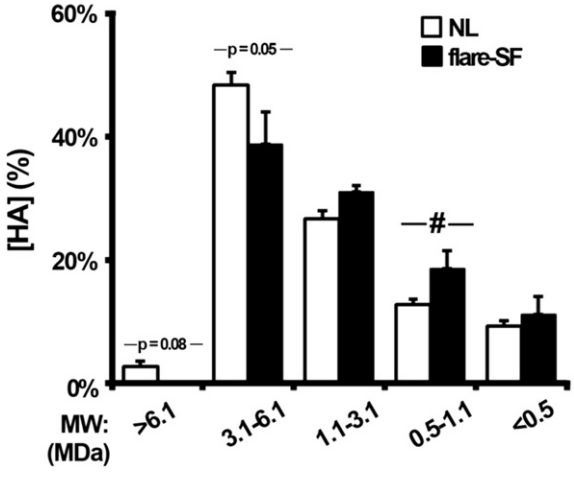

Figure 2. HAMW distribution in N=4 PRG4-deficient flare-SF samples selected for friction testing and N=14 normal (NL) SF (#= p<0.05)

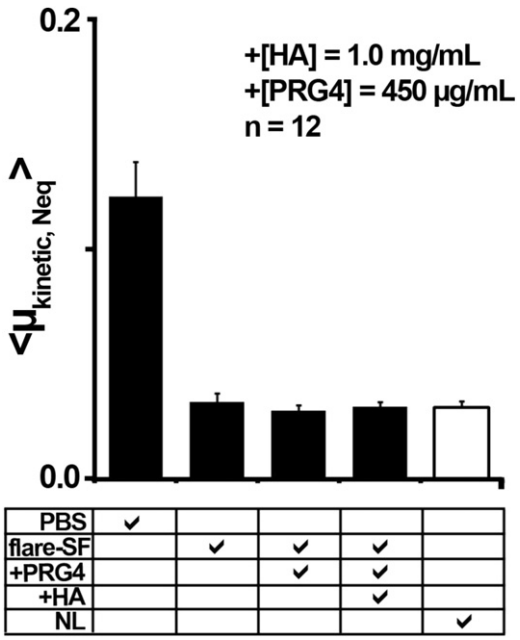

Figure 3. Kinetic friction coefficient (<µkinetic,Neq>) at Tps=1.2 s of PRG4 deficient flare-SF with 450 µg/mL PRG4 and 1.0 mg/mL 1.5 MDa HA supplementation, and NLSF.

585
CHANGE IN MRI SYNOVITIS CORRELATES WITH CHANGE IN PAIN FOLLOWING INTRA-ARTICULAR STEROID INJECTION

T.W. O'Neill [†], L.M. Forsythe [†], M.J. Parkes [†], E. Marjanovic [†], A. Gait [†], C.E. Hutchinson [‡], T.F. Cootes [†], D.T. Felson [†]. [†] *The Univ. of Manchester, Manchester, United Kingdom;* [‡] *Univ. of Warwick, Coventry, United Kingdom*

Purpose: Synovitis is a well recognised finding in knee osteoarthritis. It can be identified on Magnetic Resonance Imaging (MRI) as synovial thickening, although injection of contrast material is required to distinguish synovial tissue from synovial fluid. The aim of this analysis was to determine whether change in synovial tissue volume as assessed using gadolinium (Gd) enhanced MRI imaging correlates with change in knee pain following intra-articular steroid therapy.
Methods: Men and women aged 40 years and older who met ACR criteria for the disease, were recruited for participation in an ongoing open label clinical trial of intra-articular steroid therapy. Subjects who took part in the study had significant knee pain and grade 2 or higher knee OA. At baseline visit they completed a questionnaire about their symptoms including KOOS pain scale (100 = no pain to 0 = extreme pain) and also a VAS score (0 = no pain] to 10 = extreme pain) for pain on a nominated activity (VASnA). They subsequently had a Gd enhanced MRI immediately prior to having an intra-articular steroid injection with repeat questionnaire and Gd-enhanced MRI scan at follow up visit to assess synovial response usually within 2 weeks after the injection. To assess synovial tissue volume, sagittal (post CE T1W Fat Suppressed images: TR 500ms, TE 17ms; FoV 15.9 x 15.9cm; slice thickness 3mm) scans were obtained. Manual segmentation of the synovial tissue layer was performed on the post contrast knee image by a single observer. Using computer image analysis we excluded cartilage within the segmented space, by thresholding in the associated sagittal (3D WATSc: TR 20ms, TE 7.7ms, FoV 15cm, 288x288) scan. The rest of the segmented space was assumed to be a mixture of fluid and synovial tissue. We calculated the proportion of synovial tissue in every voxel using P = (I - mf) / (ms - mf) truncated to [0,1], where I is the voxel intensity and mf, ms are the means of the intensity distributions of fluid and synovial tissue volume respectively. We looked at mean synovial volume before and after the steroid injection and looked at the Spearman Rank correlation coefficient between change in synovial volume and change in the level of KOOS-pain and also VASnA.
Results: We analysed data from 41 patients. Their mean age was 62.4 years (SD 10.5 years), and 21 were female (51.2%). The median time between baseline and follow up scan was 9 days (IQR 7 to 14 days). The median synovial tissue volume at baseline was 7,556mm^3 (IQR 4,670mm^3 to 11,269 mm^3), and at follow up was 7,078mm^3 (IQR 3,642mm^3 to 8,541mm^3); median difference -1,007mm^3 (95% CI -1,909mm^3 to -320mm^3). Both KOOS pain (24.7pts; 95% CI 18.4 pts to 31.0 pts) and VASnA (-3.2cm; 95% CI -4.1cm to -2.2cm) improved significantly between baseline and follow up. The change in synovial tissue volume correlated with change in VASnA ($r_s = 0.39$; $p = 0.01$) though not with KOOS-pain ($r_s = -0.11$; $p = 0.50$). Change in VASnA did not appear to correlate with synovial tissue volume at baseline ($r_s = -0.03$; $p=0.85$); nor did change in KOOS pain ($r_s = 0.17$; $p=0.30$).
Conclusions: Synovial tissue volume in knee osteoarthritis, assessed with Gd-enhanced MRI correlates with change in pain assessed as pain on a nominated activity, though not KOOS, in response to intra-articular steroid injection.

586
A SYSTEMATIC REVIEW OF WHERE AND HOW TO INJECT IN THE KNEE?

N. Maricar, M.J. Parkes, M.J. Callaghan, D.T. Felson, T.W. O'Neill. *The Univ. of Manchester, Manchester, United Kingdom*

Purpose: The knee can be injected at different anatomic sites with or without image-guidance. We undertook a systematic review to determine i) the accuracy of intra-articular knee injection (IAKI) and whether this varied by site, use of image-guidance and clinician experience, and ii) whether accuracy of IAKI was linked with improved therapeutic response.
Methods: Medline, Embase, AMED, CINAHL, Web of Knowledge and the Cochrane Central Registers for Controlled Trials up to July 2012 were searched including additional hand searches of relevant articles. Studies included were those that evaluated accuracy of steroid injection at one or more IAKI sites performed either blinded or using image-guidance. We pooled data across studies to determine accuracy and also differences in accuracy by injection site when injections were delivered blind or guided by imaging. Using data from the small number of studies which permitted within-study comparisons, we performed meta-analyses (fixed effect model with forest plot) to determine differences in accuracy of blind and guided injections.
Results: Data from 26 publications were included in the review. Only 5 studies were available for within-study comparison for 4 out of the 8 injection sites. The within-study analyses found guided IAKIs at superomedial patellar (SMP), medial midpatellar (MMP), superolateral patellar (SLP) and lateral suprapatellar bursa (LSB) had greater accuracy using image-guidance than given blind [pooled risk difference 0.09-0.19]. Using between-study analyses, for blinded IAKIs, the SLP site was the most accurate [87%] though SMP and lateral sites such as lateral mid-patellar (LMP) and LSB were also accurate [pooled accuracies 82-84%]. Overall about one in five blinded IAKIs were inaccurate. Using data pooled across studies the MMP [Absolute Risk Difference (ARD) 0.22, 95% Confidence Interval (CI) 0.10-0.33] and the anterolateral joint line injection approaches [ARD 0.28, 95% CI 0.20-0.35] were least accurate when performed blinded compared to when performed guided. Overall there was no significant difference in accuracy between the lateral injection sites and the medial sites [Blinded: ARD 0.04, 95% CI 0.00 to 0.08; Guided: ARD 0.01, 95%CI -0.01 to 0.03]. Adverse events associated with IAKI at different sites were uncommon, though compared to the lateral approach, the medial approach was associated with a higher frequency of adverse events. There was some evidence that experience of the injector was linked with improved accuracy for blinded though not image-guided injections. There was no association between accuracy of IAKIs and treatment outcome though there was a paucity of data.
Conclusions: IAKIs are safe and can be accurate when performed blind depending on injection site. The use of image guidance improves accuracy of IAKI at all sites. Further studies are required to address the question whether accurate localisation is linked with a better outcome.

587
COMPARATIVE EFFECTIVENESS OF TWO HYALURONIC ACID FORMULATIONS ON PERCEIVED FUNCTIONAL PERFORMANCE

J. Zeni, Jr. [†], L. Snyder-Mackler [†], M. Axe [†,‡]. [†] *Univ. of Delaware, Newark, DE, USA;* [‡] *First State Orthopaedics, Newark, DE, USA*

Purpose: Intra-articular hyaluronic acid (HA) injections are a non-surgical treatment for knee osteoarthritis (OA) that have the potential to reduce pain and improve functional ability. Despite potential benefits,